

# Geographic Inequalities in Progress against Lung Cancer among Women in the United States, 1990–2015



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## Abstract

**Background:** Lung cancer–related death rates in the United States have declined steadily since 1990 in men but not until the mid-2000s in women, with the gap in mortality narrowing during the most recent time period. We examined variation in the declining trend among women by county, where many tobacco control policies are implemented.

**Methods:** We obtained county-level lung cancer death rates among women from the National Center for Health Statistics mortality file and calculated relative changes from 1990–1999 to 2006–2015. Optimized hotspot analysis identified contiguous counties with small declines or increases in death rates.

**Results:** We identified two distinct clusters of counties: 669 in Appalachia and the Midwest (Hotspot 1) and 81 in the northern Midwest (Hotspot 2). From 1990–1999 to 2006–2015, death rates among women increased by 13% in Hotspot

1 and by 7% in Hotspot 2 counties, while rates decreased by 6% in the non-hotspot United States. From 1990–2015, death rate ratios (RRs) in hotspot versus non-hotspot counties changed from 4% lower (RR, 0.96; 95% CI, 0.94–0.99) to 28% higher [RR, 1.28; 95% confidence interval (CI), 1.25–1.31] for Hotspot 1 counties and from 18% lower (RR, 0.82; 95% CI, 0.76–0.89) to unity (RR, 0.99; 95% CI, 0.93–1.05) for Hotspot 2 counties.

**Conclusions:** We identified areas in the Midwest and Appalachia where progress against lung cancer mortality among women has lagged compared with a steady national decline.

**Impact:** Targeted tobacco control programs could reduce the excess burden of lung cancer among women living in hotspot counties and prevent widening geographic inequity. *Cancer Epidemiol Biomarkers Prev*; 27(11); 1261–4. ©2018 AACR.

## Introduction

Lung cancer is the leading cause of cancer-related death among women in the United States, causing about 71,000 deaths annually (1). Nationally, lung cancer death rates have declined steadily among men since 1990 but not until the mid-2000s in women, with the excess risk in men narrowing during the most recent time period. This lag in the decline among women is thought to reflect historical sex differences in the tobacco epidemic, with women initiating and quitting smoking in large numbers later than men (2–5). Furthermore, the decline in lung cancer death rates among women slowed abruptly for women born around 1950s (6), which temporally coincided with an increased initiation of smoking among girls in the 1960s and 1970s (7, 8).

Several previous studies have reported inequalities in progress against lung cancer among men and women by state and region (8–10), which are thought to reflect differences in

tobacco control policies (9, 11–13). However, progress was evident in all states among men but limited to certain states among women (6). Lung cancer incidence and death rates among women began decreasing earlier and decreased faster in California, the first state to implement a statewide comprehensive tobacco control program (9, 14, 15), than other states. Little is known about recent disparities in progress against lung cancer among women across counties, where local tobacco control policies (e.g., smoke-free air laws) are implemented. In 2017, Mokdad and colleagues (16) estimated county-level death rates for major cancers, including lung cancer, by calendar year from 1980 to 2014 and mapped the total percentage of changes in death rates in 2014 from the rates in 1980. However, the analysis for lung cancer was limited because it examined mortality patterns for both sexes combined, despite the striking differences in lung cancer rates, trends, and geographic patterns between men and women (8–10). This analysis also ignored the rise, plateau, and decline of lung cancer mortality from 1980–2014 (1, 17).

In this article, we examine county-level changes in lung cancer–related death rates among women between two time periods: 1990 to 1999, when lung cancer–related death rates among women nationally were increasing or plateauing; and 2006 to 2015, when death rates were declining. We aimed to identify clusters of contiguous counties that are not benefitting from progress against lung cancer, as these counties may avail themselves for coordinated tobacco control efforts without regard for state boundaries. In the Supplementary Data, we also examine the change in lung cancer–related death rates between the two time periods by county among men.

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**Note:** Supplementary data for this article are available at *Cancer Epidemiology, Biomarkers & Prevention* Online (<http://cebp.aacrjournals.org/>).

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**doi:** 10.1158/1055-9965.EPI-17-0934

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## Materials and Methods

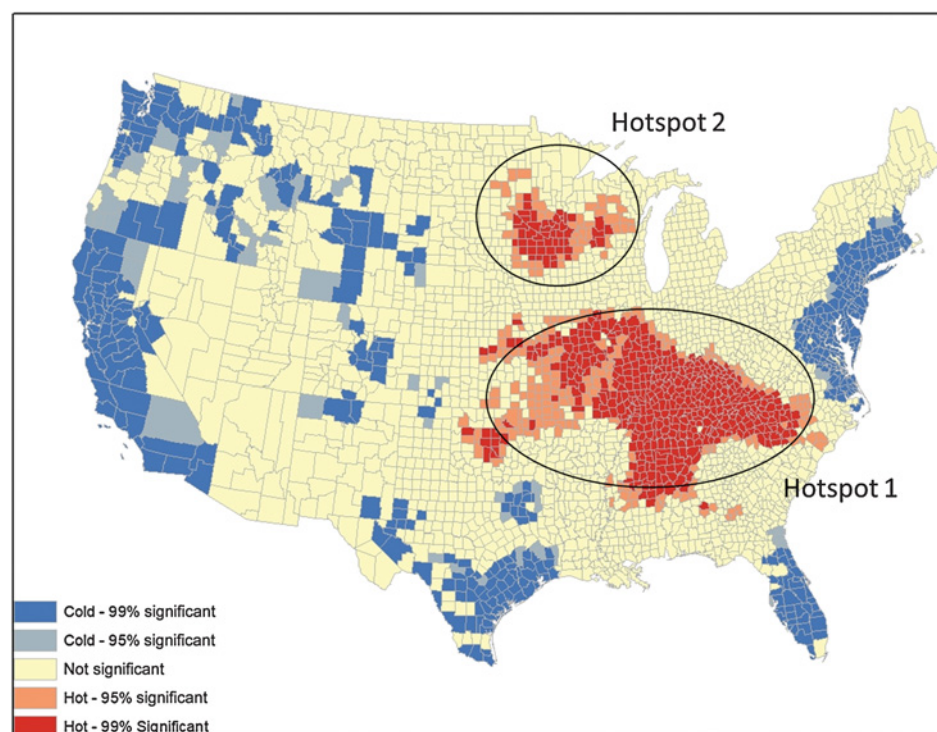
Lung cancer–related death rates were obtained from the SEER\*Stat database of the National Cancer Institute's Surveillance, Epidemiology and End Results Program, as reported by the National Center for Health Statistics (18). These data are publicly available and de-identified, and were obtained and analyzed during 2017. For each county in the contiguous United States, we calculated first age-standardized lung cancer–related death rates among women (2000 U.S. standard population) for 1990 to 1999 and 2006 to 2015 using SEER\*Stat software (19), then absolute change (2006–2015 rate minus 1990–99 rate, with 95% CI) and relative change (the absolute difference expressed as a percentage of the 1990–99 rate) between the two periods. The statistical significance of absolute change in county-level lung cancer–related death rates was assessed using rate differences and 95% confidence intervals (CIs); changes were considered statistically significant if the confidence interval did not include the null value of 0.

County-level relative changes in the lung cancer–related death rate were used as input for cluster analysis with optimized hotspot analysis (ArcGIS); the distance band used for analysis was identified on the basis of incremental spatial autocorrelation. The output from optimized hotspot analysis is a Getis-Ord  $G_i^*$  statistic, which identifies statistically significant clusters of high and low values based on the "neighborhood" of each county. Counties are assigned a Z score representing the statistical significance of the cluster, given for 90%, 95%, and 99% confidence levels. We considered clusters statistically significant at a  $P$  value of  $<0.05$  and a Z score of 1.96 (95% confidence level). As the input value for the cluster analysis was percent change, "high" clusters represented positive or small negative values of percentage change (increases or small declines in the lung cancer–related death rate between the two time periods) and "low" clusters represented

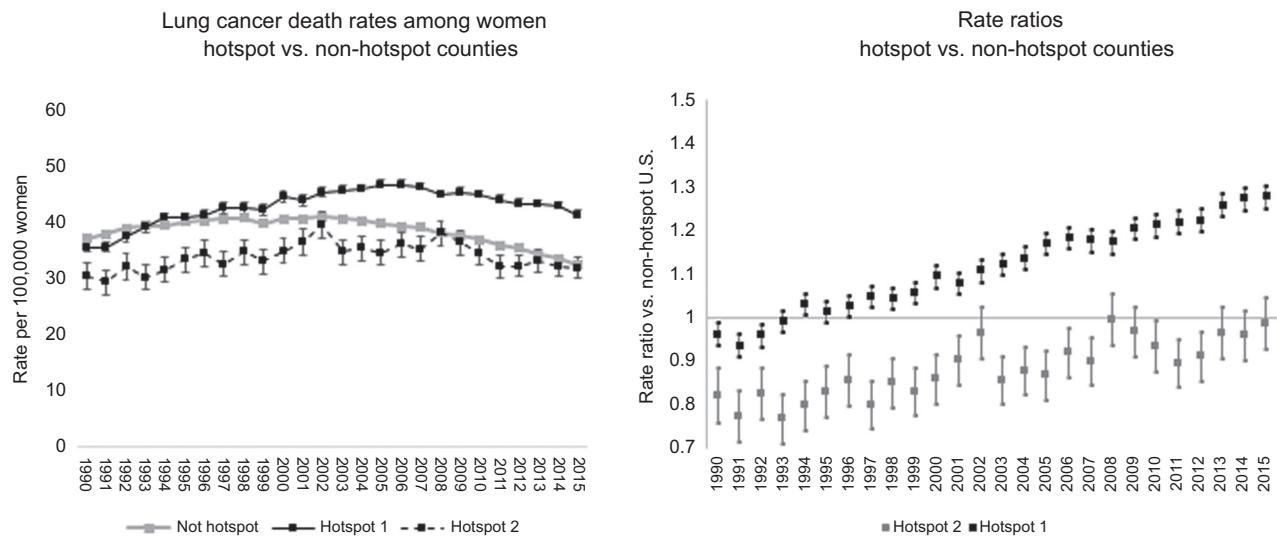
large negative values of percent change (large decreases in the rate). To compare mortality in identified hotspots and the non-hotspot United States over time, we calculated age-standardized rates, rate ratios, and their 95% confidence intervals for each identified hotspot and for the non-hotspot United States for each year between 1990 and 2015. We used joinpoint regression with a maximum of three joinpoints to analyze trends in lung cancer mortality for each identified hotspot and the non-hotspot United States. We excluded 347 counties from analysis because they had less than 10 deaths in either 1990 to 1999 or 2006 to 2015 (11.1% of U.S. counties). Demographics of identified hotspot counties were described using data from the 2010 U.S. Census. We also calculated absolute change and percent change in lung cancer–related death rates between 1990–1999 and 2006–2015 by county among men.

## Results

Of the 2,767 counties with available rates for both intervals, 336 counties experienced a statistically significant absolute decrease in lung cancer–related death rates among women, whereas 677 experienced a significant increase; among men, nearly all counties experienced a statistically significant absolute decrease (Supplementary Fig. S1). Rates increased among women in the Midwest and decreased among those living on the West Coast (Supplementary Fig. S2). Two clusters of counties with small declines or increases in the relative lung cancer death rate were identified (Fig. 1); 669 counties in 21 states located in central Appalachia and southern parts of Midwest (Hotspot 1), and 81 counties in 4 states located in northern parts of Midwest (Hotspot 2). From 1990–1999 to 2005–2016, lung cancer death-related rates rose by 13% among women in Hotspot 1 (39.7 per 100,000 in 1990–1999 to 44.8 per 100,000 in 2006–2015) and by 7% among women in Hotspot 2 (32.9 per 100,000 in 1990–1999 to



**Figure 1.** Hotspot analysis of the percentage of change in the lung cancer–related death rate among women in contiguous U.S. counties from 1990–1999 to 2006–2015. The figure contains a map of the contiguous United States. Counties that are part of a lung cancer change hotspot are in red, whereas counties that are part of a lung cancer change "cold" spot are in blue. Hotspot 1 and 2 are circled and labeled. Counties that are not a part of a statistically significant cluster are in yellow.



**Figure 2.**

Rates and rate ratios of lung cancer death rates among women in Hotspot 1 and Hotspot 2 compared with non-hotspot counties in the United States, 1990–2015. The figure contains two panels. The first (A) is a line graph of the lung cancer death rate among women, with death rate on the y axis and year on the x axis, stratified by Hotspot 1 (black solid line), Hotspot 2 (black dashed line), and non-hotspot counties (gray line). The second (B) is a line graph of the rate ratio of lung cancer death, with rate ratio on the y axis and year on the x axis, comparing Hotspot 1 with the non-hotspot United States (black bars) and Hotspot 2 to the non-hotspot United States (gray bars).

34.4 per 100,000 in 2006–2015), whereas rates decreased by 6% among women in the non-hotspot United States (39.7 per 100,000 in 1990–1999 to 37.0 per 100,000 in 2006–2015).

In the non-hotspot United States, lung cancer–related death rates among women rose from 1990 to 1995 (APC: 1.5%, 95% CI: 1.0%, 2.1%), plateaued between 1995 and 2003 (APC: 0.1%, 95% CI: –0.1% to 0.4%), and declined thereafter with the decline more accelerated during the most recent time period [from –1.2% (95% CI: –1.7% to –0.8%) during 2003–2009 to –2.5% (95% CI: –2.8% to –2.1%) during 2009–2015]. In contrast, death rates in hotspot counties continued to increase through about the mid-2000 and declined afterward, albeit slowly (Fig. 2; Supplementary Table S1). Consequently, between 1990 and 2015, the death rate ratio (RR) in hotspot counties versus non-hotspot counties changed from 4% lower (RR, 0.96; 95% CI, 0.94–0.99) to 28% higher (RR, 1.28; 95% CI, 1.25–1.31) for Hotspot 1 counties and from 18% lower (RR, 0.82; 95% CI, 0.76–0.89) to unity (RR, 0.99; 95% CI, 0.93–1.05) for Hotspot 2 counties (Fig. 2; Supplementary Table S2).

Approximately 22 million people lived in hotspot counties in 2010. Compared with the rest of the United States, hotspot counties had larger proportion of whites (87.4% white vs. 81.0%), rural residents (34.7% of residents living in a rural area vs. 18.3%), and lower educational attainment (16.4% with a college degree vs. 19.9%). Women residing in Hotspot 1 counties represented 11% of all U.S. women, but 15% (10,595/70,073) of lung cancer deaths recorded in 2015 nationally. We found similar results when we restricted the analysis to non-Hispanic white women.

## Discussion

In contrast with the steady decline in national lung cancer death rates among women since the mid-2000s (1), we identified

distinct areas of the United States where progress has lagged. Counties in our identified hotspots have trends in lung cancer–related death rates among women that are distinct from the non-hotspot United States. The excess burden of lung cancer–related mortality among women central Appalachia and southern part of Midwest compared with the national average has grown consistently since the mid-1990s. These findings expand on previous studies that have demonstrated state- and region-level disparities in lung cancer mortality (8–10) and those that considered trends in lung cancer death rates for men and women combined (16). Given the importance of cigarette smoking prevalence to lung cancer incidence and mortality, our findings are consistent with previous studies that have found Midwestern and Appalachian states have the highest prevalence of smoking among women and the lowest percent declines in smoking from 1997 to 2007 (13).

Counties in the northern part of Midwest (Hotspot 2) also experienced an increase in lung cancer death rates from 1990–1999 to 2006–2015. At the beginning of the study death rates in these counties were 20% lower than those of non-hotspot counties, but by the end of the study, rates in the two areas have become virtually identical. This in part indicates the lag in progress against lung cancer in the northern part of the Midwest and illustrates the importance of considering both relative and absolute measures of change in health outcomes. Although national organizations may prioritize areas of high relative and absolute burden of lung cancer mortality such as Hotspot 1, state and local organizations serving Hotspot 2 may be more concerned about relative trends in these counties.

The Appalachia and parts of Midwest (Hotspot counties) comprise states where both excise taxes on tobacco and spending on tobacco control measures at the state-level are very low (9, 20). For example, the state excise tax on a pack of cigarette is less than US \$1.00 in several Appalachian and Midwestern states, compared with over US \$4.00 in New York and Connecticut (21).

Most southern and Midwestern states do not have comprehensive smoke-free air laws banning smoking in the workplace, restaurants, and bars (22). Intensified efforts at the county, state, and federal level to reduce smoking prevalence among women in hotspot counties could reduce lung cancer mortality.

Additional factors that may contribute to differences in lung cancer-related mortality include geographic differences in the prevalence of occupational and environmental exposures that increase lung cancer risk, such as asbestos or radon (23). Nationwide estimates of county-level prevalence of these exposures are not available. However, we expect these differences to be small, as cigarette smoking accounts for approximately 75% of lung cancer-related deaths in women (24), and smoking-attributable cancer mortality among women is highest in southern and Midwestern states (25).

The strengths of our study include the use of advanced spatial analysis to characterize spatial and temporal trends in lung cancer-related mortality among women. To our knowledge, this is the first study to examine recent progress in reducing lung cancer-related death rates among women by county and to identify contiguous counties with high burden of disease. Limitations of the study include county-level suppression of data and ecological design.

In conclusion, although lung cancer-related death rates among women in non-hotspot counties began plateauing in late 1990s

and declined steadily afterwards, rates in parts of the Midwest and central Appalachia increased steeply until the late 2000s. Consequently, the high burden of lung cancer over this period shifted from non-hotspot counties to parts of the Midwest and central Appalachia. Coordinated, targeted public health intervention and tobacco control policies could reduce the excess burden of lung cancer among women living in these areas and prevent widening geographic inequity.

**Disclosure of Potential Conflicts of Interest**

No potential conflicts of interest were disclosed.

**Authors' Contributions**

Conception and design: K. Ross, M.R. Kramer, A. Jemal

Development of methodology: K. Ross, M.R. Kramer, A. Jemal

Writing, review, and/or revision of the manuscript: K. Ross, M.R. Kramer, A. Jemal

Study supervision: A. Jemal

**Acknowledgments**

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Received October 10, 2017; revised December 4, 2017; accepted February 6, 2018; published first March 30, 2018.

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